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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,302	ALTIERI ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-42 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-42 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~11/8/2002~~. 11/18/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II (claims 1-9 and 13-31) in the reply filed on April 21, 2004 is acknowledged. The traversal is on the ground(s) that both methods from each of Groups I and II are directed to a method of diagnosing cancer in a patient and involve detecting survivin. Upon reconsideration the Examiner has rejoined Group I (1-12 and 17-31) with the claims of Group II (claims 1-9 and 13-21) for examination. The examination will also include new claims 32-42.

The requirement is deemed proper and is therefore made FINAL.

2. Claims 1-42 are pending.

Claims 32-42 have been added.

Claims 1-42 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 17 and 21-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 17 is broadly drawn to "[a] kit for diagnosis, prognosis or monitoring cancer, comprising a container for collecting biological fluid... and an agent that detects ... survivin...". Claims 7 and 18 distinctly express that the agent may be an survivin antibody, survivin binding partner and nucleic acids that bind survivin nucleic acids. While the specification does mention some of the agents that detect survivin, the specification does not teach the broad application of any agent capable of detecting survivin or how to make and use the ambiguous agents that fall under the scope of the claim. A number of agents with different structural and binding properties could or could not detect survivin. Given the breadth of the claims, which broadly state an ambiguous agent that is to detect survivin, molecules and substances such as ribozymes and DNA mutagens cannot be excluded. In the instant case, the claims are so broadly drawn, the guidance is so limited, and the art is so unpredictable that skilled artisan is presented with a multitude of un-linked alternatives with no guidance as to which will enable use of the invention as claimed. One of skill in the art would not have a reasonable expectation of success in practicing the claimed invention and one skilled in the art would not be able to practice the claimed invention without undue experimentation.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22, 25-27 and 32-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation, CIS in claim 5 is indefinite. For examination purposes the Examiner will interpret the acronym as meaning carcinoma in situ, however this recitation could also mean for example, cis relative to the positioning of DNA elements or common input strength index. Applicants are requested to cite the entire meaning of the acronym after the first recitation of the acronym.

b. Claim 17 is vague and indefinite in the term, agent. The metes and bounds of the claim cannot be determined. An "agent" can be anything, such as a peptide, an organic molecule, an inorganic molecule, a DNA fragment, a plastic, a carbohydrate, etc. Applicant's attention is directed to Ex Parte Tanksley (26 USPQ2d 1384) wherein the Board noted that under 35 U.S.C. 112, second paragraph, the claims must be so definite as to allow the comparison with the available art and must also make it possible for the public to determine from the claim what it encompasses.

c. The recitation "a means to analyze the presence of survivin" in claim 22 is vague and indefinite. It is not clear what steps are embodied by the precise term "means". And while all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is practiced. The method steps should at least include reagents necessary for the assay, a detection step in which the reaction products are quantitated or visualized and a correlation step describing how the results of the assay allows the

determination of for example, the analysis of the presence of survivin.

d. Claims 25-27 are vague and indefinite in the recitations "comprising quantitating the amount of survivin in the sample ...from a patient and comparing the amount of survivin... in control samples to determine [stage or grade] of ...cancer". The methods lack complete steps. And while all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is practiced. The method steps should at least include reagents necessary for the assay, a detection step in which the reaction products are quantitated or visualized and a correlation step describing how the results of the assay allows the determination of for example, determining the amount of survivin. For example, it is not clear if gene copy number is being assessed or level of survivin protein.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical

Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1-4, 6-10, 13, 15, 16, 28-34 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Jouben-Steele et al. (Laboratory Investigation 1(79): 99A, January 1999/ IDS reference submitted November 18, 2002). Jouben-Steele's abstract discloses a method of diagnosing urothelial neoplasia (including bladder and prostate cancer) comprising assaying urine sediment of patients in comparison to normal control samples. Survivin mRNA was present in the urine sediment of patients as determined by RT-PCR, nested PCR and dot blot analysis.

9. Claims 1-12 and 15-42 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,656,684 (filed November 2, 2000). U.S. Patent 6,656,684 discloses a diagnostic method for predicting the recurrence of a tumor or cancer in a mammal by contacting a mammalian tissue sample with...a Survivin-specific ligand...", see column 2, lines 19-34. Inherent in the diagnostic method of evaluating the recurrence of the cancer are the methods of determining the grade of cancer, stage of a cancer, and monitoring cancer in a patient comprising quantitating the amount of survivin in a sample of biological fluid. It is clear in the establishment of the recurrence of the cancer that the grade, stage and monitoring of the cancer has been conducted. The disclosed

invention relates to tumors of the urogenital tract, as well as all types of sarcomas. The Examiner is interpreting the acronym, CIS as a carcinoma in situ and it is reasonable to conclude that the disclosed methodologies are applicable to bladder or prostate cancer graded as CIS. Provided that the disclosed invention includes "all types of sarcomas" cancers regarded as CIS would be assayed, see column 2, lines 43-45. The physiological sample may be a fluid, for example whole blood and the detection agent may be an antibody, see column 2, lines 43-48. Western blot analysis was performed, as well as immunohistochemical staining, see column 9, lines 27-60. Northern analysis or northern blotting is used in the disclosed assay to identify survivin RNA sequences using a nucleic acid probe, see column 8, lines 1-25. The present invention also provides a diagnostic kit for predicting recurrent of tumor or cancer in a mammal, containing packaging material, a Survivin-specific ligand, a pro-apoptosis factor (PAF)-specific ligand and instructions directing the use of the aforementioned items, see column 2, lines 49-54.

Claim Rejections - 35 USC § 103

10. Claims 1-4, 6-10, 13-24, 28-32, 41 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouben-Steele et al. (Laboratory Investigation 1(79): 99A, January 1999/ IDS reference submitted November 18, 2002), in view of Bio-Rad Laboratories Catalog 1998/99. The teachings of Jouben-Steele have been presented in the 102(b) rejection, see paragraph number 8. Jouben-Steele does not teach wherein

the dot blotting utilizes a Bio-Dot SF module or a kit for diagnosis, prognosis or monitoring cancer, comprising a container for collecting biological fluid from a patient.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize the Bio-Dot SF (slot format) microfiltration unit. One of ordinary skill in the art would have been motivated to use this particular microfiltration and screening equipment because it provides a reproducible method for nucleic acid in solution onto nitrocellulose and provides information on a target transcript and gene expression.

Furthermore, although the claims recite a kit and a container for use, no positive recitation of the kit ingredients/elements distinguishes the claim over the reference. Therefore, the reference reads on the claimed kit and container of use. It is noted that kits traditionally include structural material such as instructions, labeling and promotional material. The container is viewed as a recitation of intended use and therefore is not given patentable weight in comparing the claim with the prior art. See MPEP 706.03(a). Thus the container for use included in a kit or article of manufacture constitutes an "intended use" for that kit or article of manufacture. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit containing a compound which selectively detects survivin and a kit for use. One of ordinary skill in the art would have been motivated to make a kit because test kits including compounds are packaged for the

advantages of convenience and economy for the ordinarily skilled artisan or the practitioner. Kits are conveniently made to reproducibly obtain results under test conditions and it is conventional to assemble necessary reagents including compounds, such as nucleic acid probes to selectively hybridize to nucleic acid molecules such survivin DNA for the convenience of the practitioner and commercial expediency.

10. Claims 1-13 and 15-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jouben-Steele et al. (Laboratory Investigation 1(79): 99A, January 1999/ IDS reference submitted November 18, 2002), in view of U.S. Patent 6,656,684 (filed November 2, 2000). The teachings of Jouben-Steele have been presented in the 102(b) rejection, see paragraph number 8. Jouben-Steele does not teach wherein the bladder or prostate cancer is graded as CIS, the cancer is diagnosed using an immunoassay, a kit for diagnosis, prognosis or montoring cancer including all the elements for detection of the presence of survivin in a biological fluid.

However, U.S. Patent 6,656,684 teaches a diagnostic method for predicting the recurrence of a tumor or cancer in a mammal by contacting a mammalian tissue sample with...a Survivin-specific ligand...", see column 2, lines 19-34. Inherent in the diagnostic method of evaluating the recurrence of the cancer are the methods of determining the grade of cancer, stage of a cancer, and monitoring cancer in a patient comprising quantitating the amount of survivin in a sample of biological fluid. It is clear in the establishment of the recurrence of the cancer that the grade, stage and monitoring of the cancer has been conducted. The patent relates to tumors of the urogenital tract, as well as all types of sarcomas. The Examiner is interpreting the

acronym, CIS as a carcinoma in situ and it is reasonable to conclude that the disclosed methodologies are applicable to bladder or prostate cancer graded as CIS. Provided that the patent includes "all types of sarcomas" cancers regarded as CIS would be assayed, see column 2, lines 43-45. The physiological sample may be a fluid, for example whole blood and the detection agent may be an antibody, see column 2, lines 43-48. Western blot analysis was performed, as well as immunohistochemical staining, see column 9, lines 27-60. Northern analysis or northern blotting is used in the disclosed assay to identify survivin RNA sequences using a nucleic acid probe, see column 8, lines 1-25. The present invention also provides a diagnostic kit for predicting recurrent of tumor or cancer in a mammal, containing packaging material, a Survivin-specific ligand, a pro-apoptosis factor (PAF)-specific ligand and instructions directing the use of the aforementioned items, see column 2, lines 49-54.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to diagnose, stage, grade and monitor a bladder or prostate cancer of pathological phase and implement a kit comprising all the elements of capable of allowing the selective detection of survivin. One of ordinary skill in the art would have been motivated by the teachings of both references that the assessing of the survivin in any cancer is possible and practictioners package test kits including all the required compounds for the advantages of convenience and economy for the ordinarily skilled artisan.

11. Claims 1-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,656,684 (filed November 2, 2000), in view of Bio-Rad Laboratories Catalog 1998/99. The teachings of the patent have been presented in the 102(e) rejection, see paragraph number 9. The patent does not teach that the survivin was detected by dot blotting comprising the use of a Bio-Dot SF module.

However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize the Bio-Dot SF (slot format) microfiltration unit. One of ordinary skill in the art would have been motivated to use this particular microfiltration and screening equipment because it provides a reproducible method for nucleic acid in solution onto nitrocellulose and provides information on a target transcript and gene expression.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The examiner works a flexible schedule, however she can usually be reached between the hours 6:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (703) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
12 July 2004